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REGULATIONS ON GENETICALLY MODIFIED MICROORGANISMS & THEIR RELATION TO BIOTERRORISM IN INDIA

Gurvinder Singh[1*], Vikas Budhwar[1], Manjusha Choudhary[2] and Sikander Singh[3]

[1]*Department of Pharmaceutical Sciences, Maharshi Dayanand University, Rohtak, 124001, Haryana, India*
[2]*Institute of Pharmaceutical Sciences, Kurukshetra University, Kurukshetra, India*
[3]*Aimil Pharmaceuticals Ltd., New Delhi, India*

Covid-19, a virus-driven pandemic, has shown the world the possible dangers posed by microorganisms like bacteria, viruses, rickettsia, fungi, and their toxins. However, genetically engineered microorganisms are helpful in various biosciences fields, including medication, horticulture, and fundamental investigation into life processes. Among these, some genetically altered microorganisms have drastic potential to cause harm to humans, and the environment, like the current coronavirus pandemic has shaken the world with fatalities caused by it worldwide and crashed the global economy. On the one hand, genetically engineered organisms help understand the ultrastructure of these organisms and as a tool to combat the disease caused by them. On the other, the increasing research on this also poses a threat to the occurrence of pandemics throughout the world. In India, genetically altered microorganisms are regulated by the Rules, 1989 under sections 6,8 and 25 of the Environment Act, 1986. Bioterrorism is the systematic and deliberate deployment of hazardous organisms such as bacteria, viruses, or toxins to spread infectious diseases on a massive scale to wipe out a vast population.

The global incidents of the recent twenty years presented that the danger of biological fighting isn't a fictional thing yet a harsh truth. Hazardous microbes can be utilised in bioterrorism by seeing flare-ups brought about by microorganisms. So, there is a need to improve the countermeasures to tackle the spread of infectious diseases. This review covers the various regulations for genetically altered microorganisms in India regarding their sale, import-export storage, and creation, emphasising regulating bodies; their constitution, and application forms for the registrations and approval for research on such microorganisms, and this assessment presents a clear overview of the country's probable biothreats, current laws, and regulations to combat such incidents, with a significant necessity for their execution, and biodefense measures for readiness and defence, in favour of making India a bioterror-free country.

Keywords: *Genetically Modified Organisms (GMOs), Genetically Engineered(GE), Biosafety Level(BSL), Bioterrorism, Biowarfare*

INTRODUCTION

GMOs and GMMs are organisms, and microorganisms whose hereditary content (DNA) is deliberately altered in ways that do not occur naturally via mating or recombination. The technique is known as " rDNA technology" or "genetic engineering." It is often referred to as "modern biotechnology" or "gene technology." It permits the transmission of particular genes from one creature to another, even across unrelated species[1].

In the recent 30 years, the capacity to adjust explicit qualities in genes of microorganisms has reformed various biosciences fields, including medication, horticulture, and fundamental investigation into life processes. Although, these innovations raise worries about the potential risks presented

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*Corresponding author: Gurvinder Singh, E-mail: gurvinder0036@gmail.com

by the genetically altered microorganism because many of these are hazardous due to their infectious nature to humans and the environment. So, explicit conventions have been created to securely screen the utilisation of hereditarily altered dangerous organisms because these can potentially cause mass destruction of life globally, like the Cartagena Protocol on Biosafety[2].

Genetically altered microorganisms incorporate bacteria, viruses, rickettsiae, fungi, or their toxins in which hereditary material has been modified primarily through recombinant DNA innovation that doesn't occur naturally[2].

Pharmaceutical companies are increasingly using GMMs in the development of new products. Due to recombinant technology, the development and production of new vaccines have been revolutionised. GMMs can introduce immunogenic material (antigens) into the immune systems of humans and animals to elicit an immunological response. GMM-based technology could lead to new treatments for malaria, TB, AIDS, and other developing illnesses. These new technologies open the door to producing vaccinations in various medical fields. Vaccine development and manufacture must respond quickly to existing or emerging outbreaks. Vaccination is still the most effective way to combat infections. The discovery of innovative vaccinations and their use in epidemics, on the other hand, is still limited particularly during the 2015 Ebola outbreak and the current coronavirus disease pandemic (COVID-19)[3].

Several commercial medications are complex proteins and need 3D structures to function correctly. Animal cells have unique machinery for building complex structures. Genetically modified animals/cells (transgenic, GMO) are used as "bioreactors" to produce these medications significantly. Animal products such as milk, egg white, blood, urine, and silkworm cocoons are utilised to create complex pharmaceuticals that cannot be manufactured chemically[4].

Global events during the last 20 years have shown that the threat of biological warfare isn't just a scary fantasy, but a terrible reality. They may be used in bioterrorism by monitoring flare-ups caused by microbes[5].

Bioterrorism is a genuine danger to all nations' security. Significant legal and biodefense policies must be implemented to prohibit the creation and deployment of lethal bioweapons. India is susceptible to bioterrorism attacks due to past biological warfare incidents, due to its dense population, and pleasant weather conditions[6].

In order to ensure protection from bioterrorism and safety with regard to research on GMOs India is signatory to the Biological Weapons Convention and Cartagena Protocol on Biosafety developed by the United Nations.

Cartagena Protocol On Biosafety

The Cartagena Protocol on Biosafety was developed by the United Nations (UN) to oversee the developments of LMOs or GMOs, which are emerging as a result of modern biotechnology, beginning in one country and spreading to others. The Protocol has been created in light of related worries due to GMOs which might adversely affect biodiversity and human well-being. It is an endeavour to create a universally fit system for biosafety to guarantee the protected utilisation of current biotechnology. It was adopted on January 29, 2000, and went into effect on September 11, 2003[7].

The CBD was initially booked to be concluded and adopted in the city of Colombia. Due to some reasons, the Protocol was adopted in January 2000 in Montreal. It went into power on September 11 2003, after 50 parties endorsed it.

The Contracting Parties agreed to consider the need to promote appropriate approaches for the safe transfer, maintenance, and utilisation of any genetically altered organisms resulting from biotechnology that may harm human and environmental health. In CBD protocol, the:

- Article 19(3): Requires Parties to direct, oversee or control hazards related to LMOs.
- Article 8(g): Require Parties to set up homegrown administrative and authoritative measures.
- Article 19(4): Creates commitment for Parties to the CBD to give data on any LMO moved to another party.

States and local monetary coordination associations that joined the Protocol and consent to be legitimately bound by its arrangements are designated as "parties" to the Protocol. Only Parties to the CBD can become Parties to the Protocol on biosafety. As of February 2017, 170 nations have approved this

Protocol. India is a Party to the CBD, having endorsed the convention on January 23, 2003. India is additionally a Party to CBD[7].

Rules, 1989

India has a well-ordered and organised administrative structure for biosafety assessment of hereditarily altered creatures and items thereof. India was one of the primary countries that developed the biosafety organisational framework for genetically modified microorganisms in 1989[8].

Under the powers given by Sections 6, 8, and 25 of the EPA, 1986, and with the end goal of securing the climate, nature, and well-being of humans and the environment regarding the utilisation of innovation on genetically altered microorganisms, the Central Government implemented the 'Rules for the Use Manufacture, Export-Import, and Storage of Genetically Engineered Organisms or Hazardous Microorganisms or Cells, 1989 on December 5 1989[9].

As per EPA, 1986 under the:

- Section 6, the Govt. can provide rules for techniques and safety measures for treating hazardous substances and forbids and limits the treatment of risky substances in various regions of India.
- Section 8, no one can deal with hazardous substance unless it conforms to such safety guards as prescribed.
- Section 25, the Central Govt. has the power to make rules concerning the safety and handling of hazardous substances[10].

Under EPA, 1986, "Hazardous Substance" signifies any substance or formulation that, because of its synthetic or physicochemical properties or management, is at risk of hurting people, other living animals, plants, microscopic life forms, property, or the climate[10].

Under Rules 1989, the

- "Gene Technology" signifies the utilisation of a quality strategy called recombinant DNA technology/genetic engineering, which incorporates self-cloning and removal of genes and the hybridisation of cells. The ongoing research for rDNA technology is gaining pace, and the use of microorganisms is an integral part of it. Hence the occurrence of pandemics in the future, either accidentally or intentionally by the concerned lab, cannot be ruled out. The world's key agencies are now serious about addressing this issue[8].
- "Genetic engineering" signifies a procedure through which genetic material that doesn't usually exist in microbe or cell concerned is created outside the body of the organism or cell is embedded into the taken cell or living being. This is like producing new blends of hereditary substances by combining a cell into a host cell of the microorganism and as modified life forms or in the cell by deleting parts of the heritable material[8].
- The production of living cells with novel combinations of genetic information by fusing two or more cells using procedures that do not occur naturally is referred to as "cell hybridisation."[11].

Applications of Rules, 1989

These regulations apply to the :-

- Creation, import, and storage of genetically modified microorganisms and cells.
- Genetically engineered microorganisms or organisms and cells or any other products like food, etc., containing such cells, organisms, or tissues[12].

In addition to those stated above, these restrictions apply to organisms and cells formed by using gene technologies and substances and products of which such organisms and cells are a part. These regulations will apply in the following situations:

1. Selling or storing and any other type of handling with or without consideration.
2. the export and import of genetically modified microorganisms
3. In the GMOs manufacture, packaging, and repackaging, drawing off, processing, storage & import.
4. Drug and pharmaceutical manufacturing, tanneries, distilleries

and food processing, and other industries that utilise microbes or genetically altered microorganisms[12].

The degree of Rules, 1989 is comprehensive. It covers the area of research that includes a vast scope of treatment of dangerous microbes, genetically engineered living beings, or the cells and items from these genetically altered microbes. Execution of the Rules in the whole country is regulated by six bodies which:

- Regulates and supervises safe research on dangerous microorganisms and genetically engineered creatures.
- Regulates and supervises massive scope utilisation of genetically engineered entities in manufacturing activities.
- Importation, exportation, and relocation of dangerous microorganisms, GE organic entities, and items thereof.
- Dispense of genetically engineered life forms and items from these microbes in ecological use as per legal arrangements12.

Implementation of Rules 1989

The following six committees were constituted in India to implement the rules 1989 throughout the country:

1. Recombinant DNA Advisory Committee(RDAC)
2. Institutional Biosafety Committee(IBSC)
3. Review Committee on Genetic Manipulation(RCGM)
4. Genetic Engineering Appraisal Committee(GEAC)
5. State Biotechnology Coordination Committee(SBCC)
6. District Level Committee(DLC)[12].

Recombinant DNA Advisory Committee (RDAC)

The RADC periodically examines biotechnological advancements at the national and international levels and offers suggestions for acceptable and adequate safety requirements in India for recombinant research and applications. This committee work under the guidance of the biotechnology department[9].

Review Committee on Genetic Manipulation(RCGM)

RCGM works under the DBT and keeps an eye on the current study's safety criteria and activities concerning genetically modified hazardous microorganisms. The RADC includes a: -

- CSIR(Council of Scientific and Industrial Research) representative
- ICMR(Indian Council of Medical Research) representative
- DBT(Department of Biotechnology) representative
- ICAR(Indian Council of Agricultural Research) representative
- Other experts in their capacity.
- The RCGM may appoint subgroups.

It issues guidelines manuals outlining the regulatory procedures for research using genetically altered organisms to investigate and use in the industry to protect the environment. All current investigations involving high-risk categories and controlled field trials must be evaluated to ensure that the safety and containment requirements are satisfied[9].

Institutional Biosafety Committee(IBSC)

An occupier or anybody else, including research organisations, can constitute the panel that deals with microorganisms and genetically modified organisms. The committee comprise:

- Institution's Head
- rDNA Scientist
- an expert in medicine and
- a nominee of the DBT

The occupier or any person managing microorganisms or genetically designed microbes, including research facilities, shall prepare an up-to-date on-site emergency plan following RCGM handbooks, with the support of IBSC, and should provide data to the Genetic Engineering Approval Committee, District Level Committee or State Biotechnology Coordination Committee[9].

Genetic Engineering Approval Committee(GEAC)

From an environmental aspect, the body functions as a committee within the Department of Environment, Forest, and Wildlife to authorise activities involving the large-scale use of harmful microorganisms and recombinants in research and commercial production. The Committee will also be responsible for licensing applications for releasing GMOs and items into the environment and field trials. The Committee's composition will be as follows:-

- Chairman- Additional Secretary, Department of Environment, Forests, and Wildlife
- Co-Chairman- Representative of DBT
- Members: Representatives from
- Ministry of Industrial Development,
- Department of Biotechnology and
- Department of Atomic Energy
- Expert members:
- Director General ICAR,
- Director General-ICMR
- Director General-CSIR
- Director General-Health Services, Plant Protection Adviser,
- Directorate of Plant Protection, Quarantine, and storage,
- Chairman, CPCB(Central Pollution Control Board) and
- Three outside specialists, each in their own right.
- Member Secretary: A Department of the Environment, Forestry, and Wildlife representative.
- Other members/experts may be co-opted by the committee as needed.

Under the Environment Act, the committee or any person/s authorised by it has the authority to take punitive action[9].

State Biotechnology Coordination Committee (SBCC)

Wherever required, the states should have an SBCC. SBCC study, investigate, and take disciplinary action in situations of statutory infractions through the Department and the State Pollution Control Board or Directorate of Health or Medical Services. Regularly, the committee evaluates the safety and control processes at the different facilities or organisations that handle GMOs. The Coordination Committee will be made up of the following members:-

- Chief Secretary – Chairman
- Secretary, Department of Environment – Member Secretary
- Secretary, Department of Health – Member
- Secretary, Department of Agriculture – Member
- Secretary, Department of Industries and Commerce – Member
- Secretary, Department of Forests – Member
- Secretary, Department of Public works/Chief Engineer, Department of Public Health Engineering – Member
- State microbiologists and Pathologists – Member
- Chairman of State Pollution Control Board
- The Committee may co-opt other members/experts as necessary[9].

District Level Committee (DLC)

Wherever required, DLC should be established in the districts under the supervision of the District Collectors to oversee the safety rules in facilities that use genetically altered organisms and their environmental applications[9].

The DLC or anyone appointed by it can inspect any facility participating in operations incorporating GMOs and compile an information chart, determine the dangers related to these setups, and work collaboratively in an emergency. The SBCC & GEAC receives a report from the DLC regularly. The DLC comprises:

- District Collector – Chairman
- Factory Inspector – Member
- A representative of CPCB – Member
- Chief Medical Officer (District Health Officer) – Member (Convenor)
- District Agricultural Officer – Member
- A delegate from the Department of Public Health Engineering– Member
- District Microbiologists pathologist (Technical expert) – Member

- Commissioner Municipal Corporation – Member
- As needed, the Committee may co-opt additional members/experts[9].

Indian Biosafety Regulatory Framework

All the committees constituted to implement the rules 1989 which work to ensure the conformity to the Biosafety Protocol throughout the country. The IBSC is the main body for applying the biosafety regulatory framework inside an institution.

Each organisation involved in exploration, utilisation, and operations related to genetically altered organisms and hazardous microbes must form an IBSC under Rules 1989. The biosecurity regulatory framework is implemented by the IBSC, which is the nodal agency inside an organisation. Registration and monitoring of IBSCs have been assigned to DBT/RCGM[13].

IBSC is exclusively responsible for the following:-

- At the institutional level, to execute and act to institutional biosafety and biosecurity, and
- Evaluation of recombinant DNA engineering work, including genetically altered organisms and non-genetically altered harmful microorganisms in an organisation's applications/reports[13].

Responsibilities of IBSCs

The following sections describes the working responsibilities of IBSCs and precautions taken by it:

1. It evaluates and generally supervises the research institutions, activities, and specialists indulged in HMOs(Hazardous Microorganisms) or GMOs or LMOs and GE(Genetically Engineered) investigation and ascertains the presented risk management emergency plans & risk assessment are satisfactory.
2. It counsels the PI and researchers on problems concerning biosafety in the research involving HMOs/GMOs/LMOs and GE microorganisms.
3. It informs the lead investigator of IBSC application evaluation, acceptance, or rejection.
4. Rules 1989 stipulate that copies of the site emergency plan be filed to the RCGM, GEAC, SBCC, or DLC. It inspects laboratories using a checklist and reports any incorrect measures to the organisation's leader, and keeps a record of the inspection report.
5. Any mishappening inside an institution, like non-compliance with biosafety requirements, biosecurity concerns, or severe research-related incidents or infections, must be notified to the IBSC/ RCGM[14].

Functions of IBSCs

The primary responsibility of IBSC is to carry out and ensure that the Rules of 1989 are followed at the institutional level. **Figure 1** depicts these functions[14].

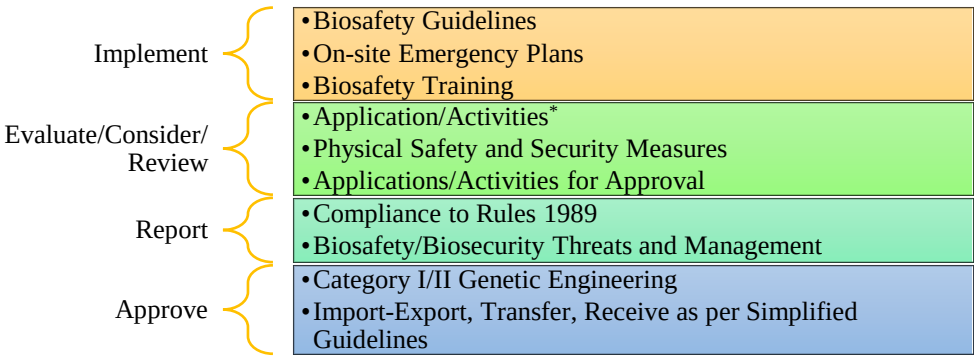

Fig. 1: Functions of IBSC.[14]

*Activities include- export, receive, transfer, import, contained (laboratory) & confined research & development involving GE organisms and/or hazardous microorganisms.

IBSC Records

The IBSC must preserve paper and digital copies of the following records:

- Authorised and formally signed observations of IBSC gatherings with attendance list.
- Annual report summarising all active GE microorganisms studies.
- IBSC copies of submissions that have been reviewed and approved.
- Applications are directed to either the RCGM or the GEAC.
- Conflict of interest declarations and confidentiality agreements signed by members are among the other documents[14].

Risk Groups and Containment Facilities

Biosafety begins through proper containment or confinement to guarantee that the working area (whether it's a laboratory, institution, or open field) is healthy for the workers, the general community, and the environment. Containment is a collection of facilities, strategies, and processes for managing and preserving dangerous microbes, genetically modified organisms, or cells in order to minimise exposure and prohibit their release within the institution and/or into the environment. The microorganism's danger category determines the type of containment facility used. The Risk Groups, as well as the microorganisms that fall into any category and the required containment facilities for each group, are listed in "The Regulations and Guidelines for Recombinant DNA Research & Biocontainment, 2017." The provided list is intended to be indicative rather than exhaustive and will be updated regularly. When dealing with organisms that aren't covered by these recommendations, the investigator should consult the IBSC/RCGM to determine appropriate risk categories and containment levels[12]. As commanded in Rules 1989, the RCGM updated "Recombinant DNA Safety Guidelines, 1990", and revised "Guidelines for Safety in Biotechnology, 1994" and framed "Guidelines on Biosafety of Recombinant DNA Research and Biocontainment, 2017". These rules depend on the latest logical data, advanced practices and the practical knowledge acquired when developing biosafety containment facilities in the country[12].

Risk Groups of Microorganisms

In the case of GMOs, pathogenicity is critical for risk analysis and successive classification. The host's potential to fight or regulate the infection determines a microbe's ability to reproduce in the host, which leads to illness.

Microorganisms are classified into danger groups based on the following parameters. (see Table 1):

Table 1: Category of experiments, GMOs involved, and Biosafety Level Facility Requirements[12].

Organic Entity	Laboratory	Levels
Microorganisms	BSL-Biosafety Level	Biosafety Level -1 to Biosafety Level -4
Animal	ABSL-Animal Biosafety Level	Animal Biosafety Level -1 to Animal Biosafety Level
Plant	PBSL-Plant Biosafety Level	Plant Biosafety Level -1 to Plant Biosafety Level -4
Insects/Arthropods	IBSL-Insect Biosafety Level	Insect Biosafety Level -1 to Insect Biosafety Level -4
Aquatic organisms	AqBSL-Aquatic Organism Biosafety Level	Aquatic Organism Biosafety Level -1 to Aquatic Organism Biosafety Level 3

(a) The organism's pathogenicity to people, animals, and plants.
(b) Methods of spreading and the microbe's host range.
(c) The presence of efficient preventative or medical therapies.
(d) Possibility of causing epidemics[12].

Data Required for GMO Safety Assessment

IBSCs must assess the safety of each application based on scientific knowledge and experience. The following are some logical

processes that should be followed while reviewing a project proposal for IBSC safety evaluation. It should be emphasised that this list is merely indicative, and specific additions, deletions, or alterations will be made to meet each project's particular needs of each project[14].

1. Details on Molecular Biology

- Source (donor) Microbe Character Traits
- Characteristics of Host/Recipient
- Organisms
- Characteristics of Gene Construct
- Characteristics of Vector and Method of Transformation
- Characteristics of Transformed/Modified Organism

2.Human and Animal Health Considerations

- Key Components - Modifications in critical nutrients, toxins or anti-nutrients, secondary metabolites, physiologically active compounds, and so on.
- Toxicity
- Allergenicity
- Nutritional analysis

3. Environmental Considerations

- Variations in development, habits, life cycle, biomass, reproduction features, responses to biotic and abiotic stresses, aggression possibility and weedy traits, non-target negative consequences, and so on.
- Disposal of biological material

On-site Biosafety & Emergency Plan

The IBSC must approve an up-to-date on-site biosafety and emergency plan for every project, in line with the RCGM's instructions and recommendations, before initiating any recombinant DNA research. The IBSC should deliver copies of the most recent on-site biosafety and an emergency plan to DLC/SBCC and GEAC. Containment/Storage of Hazardous Microorganisms/GE Organisms, as well as the storage facility and related materials, health and medical surveillance, decontamination and disposal, and emergency protocols, should all be included in the plan[14].

Accidental Release and Reporting of Incidents

Any incident within an organisation, such as violations of biosafety regulations, biosecurity concerns, or substantial study incidents and diseases, must be informed to the chairperson of IBSC within 24 hours by the PI. Within 48 hours after the event, the Member Secretary – IBSC/Chairperson IBSC must notify the accident to the DBT representative and the RCGM. The DBT candidate is responsible for evaluating the incident and submitting an impartial report[14].

Addressing Non-Compliance

IBSC will guarantee that HMOs, GE Organisms, and associated materials are stored and handled in compliance with the "Regulations and Guidelines for Recombinant DNA Research and Biocontainment, 2017" conditions. Moreover, an on-site emergency plan must be prepared, including a thorough understanding of the organisms being handled and extensive protocols to follow while dealing with them. To ensure that the assigned risk category is met, the essential safeguards against unauthorised entry and employee mobility in prohibited areas of the institution should be in place[14].

The IBSC may take several of the following actions in the case of non-compliance:

1. The usage of genetically altered microorganisms can be prohibited.
2. The permission for the use of GE materials can be revoked.
3. GE materials are seized and/or incinerated.
4. Any action considered required to safeguard the people, and the environment involves the cessation of all scientific work.
5. The RCGM should be notified[14].

Registration of IBSC at IBKP (Indian Biosafety Knowledge Portal)

Under the Rules 1989, any organisation dealing with GE microorganisms must establish an IBSC and register it with the DBT through the IBKP. The establishment will be disqualified from performing any rDNA operations or studying dangerous microbes that come within the ambit of Rules 1989 unless the IBSC is registered/renewed. Any changes to an enrolled IBSC's information and IBSC renewal must be done through IBKP. Only the organisation's highest authority or their

designee (preferably a competent senior officer) who will act as the Chairman will be able to enrol the establishment online at IBKP[13].

For an IBSC to be registered on the IBKP site, the following two processes must be accomplished:

- **Step 1 - Organisation registration:** Any organisation interested in forming an IBSC must first register with the IBKP website. Each Institution will receive a unique login ID through email when the data have been verified. This step is required for IBSC enrolment.
- **Step 2 - IBSC registration:** The institution should submit a form for IBSC enrolment on the IBKP website using the institution's fixed username and password created by the institution's relevant authority or his/her designee. The form should contain short data and authorisation documents of potential IBSC participants, comprising DBT candidates; planned operations using dangerous microbes, GE microorganisms, and their items; and the presence of containment/confinement measures to facilitate the required investigation [13].

The application will be reviewed when the information in the registration form has been verified, and the suitable judgment will be notified to the institution via the website. If there are any flaws or improvements, they will be reported to the institution via the site. The registration would be effective for three years and will need to be renewed after that time. Only after successfully registering with the IBSC may you submit an application using this site. Multiple login ids may be created by the registered IBSC's highest authority [13].

Indian Biosafety Knowledge Portal (IBKP)

The DBT has established the IBKP as part of the Government of India's Digital India effort to make regulatory processes online and paperless. DBT's website hosts the IBKP. The IBKP hyperlink is available on the DBT website that can be accessed by the following links; (http://dbtindia.gov.in/ or https://ibkp.dbtindia.gov.in)[13].

The IBKP serves as a forum for all stakeholders, including applicants, IBSC members, and RCGM members, by providing information on:

- ✓ Rules & regulations in India that are relevant to GMO/LMO biosafety.
- ✓ Biosafety, Biocontainment, and Checklists are all topics covered in these guidelines.
- ✓ RARMPs, i.e., Scientific Risk Assessment and Risk Management Plans, are included in the database on different active research operations on GMOs or LMOs and items thereof in the nation.
- ✓ Connections between global developments and scientific data.
- ✓ Annual compliance records and IBSC registrations/renewals.
- ✓ Online application forms for Import, Export, R& D projects, Pre-clinical toxicity of rDNA derived biosimilars and IND, Biosafety Research Level 1 trial, and other applications, as well as online tracking status of the application.
- ✓ Module that shows the processes of an online transaction[13].

Submission of Application Forms at the IBKP Portal

Principal Investigators should register online by filling out the appropriate application form before commencing research at the institution. On the IBKP website, you may find the application forms. The online registration forms must be completed and submitted to the facility's IBSC, which will then be evaluated by the RCGM[14].

All forms are informal, allowing applicants to input the application's critical data, as well as any necessary attachments, in the appropriate application proforma. The list of application forms or proforma available on the IBKP website is given below in Table 2[13].

Table 2: RG Classification[12].

Risk Group	Description
RG 1	Microbes that will probably not cause plant /creature/ human illness.
RG 2	Microbes that will induce illness in plant/creature/human, however, research Centre openings could conceivably make genuine contamination to individuals, and the risk of the spreading is restricted.
RG 3	Microbes that typically induce danger to plant/creature/human sickness yet doesn't conventionally spread starting with one contaminated individual then onto the next.
RG 4	Microbes generally cause dangerous/deadly human/creature/plant infections, and those will promptly spread one individual then onto the next, straightforwardly or in a roundabout way.

Sub-User Access at IBKP Portal

Because work involving genetically modified microorganisms that require IBSC and/or RCGM authorisation may include numerous investigators, the gateway contains a feature that allows the Chairman of IBSC to grant investigators sub-user admin privileges to the application forms. The following are the key aspects of sub-user website access:

The Chairperson/ Member Secretary of the IBSCs, who has authorisation to the IBSC's login ID, may permit principal investigators to the site to browse and fill out application forms.

1. Other sub-users will not be able to see data provided by a Sub-user (PI). All entries made by sub-users, on the other hand, will be available to the administrator who has the unique IBSC access ID and password.
2. Sub-user would not allow for any additional functions, such as changing IBSC data or submitting conformity reports.

On the dashboard of the RCGM website, the applicant must first pick the suitable field and then the suitable application form related to the desired purpose[14].

Online Submission of applications at IBKP

1. To begin the digital application process, the applicant must log in to the RCGM dashboard using sub-user login details and select the 'submit new application' option.
2. The form would be automatic save from time to time to prevent the loss of data entered throughout the procedure, or the user can save the file at any moment.
3. Occasionally, the Member Secretary of the IBSC should construct a strategy that includes all of the applications completed by sub-users and disseminate the strategy, together with all applications, one week prior to the IBSC meeting.
4. After the IBSC protocol has been accepted, the Member Secretary must complete the IBSC approval paperwork and upload the IBSC protocol before applying the RCGM for evaluation (preferably about a week before the session but no more than 15 days).
5. Only a filled registration form will be considered for evaluation. The applicant is accountable for ensuring that the information provided on the form is accurate. After the info has been uploaded, it cannot be changed.
6. Upon successful submission, the client will be contacted through an authorised email address, which will also be shown on the site's notification bar.
7. Every request will be assigned a UAC code, i.e. Unique Authorization Code, which the client can use to check the status of their application at IBKP[14].

Approval of Application Forms by Competent Authorities

According to the Rules of 1989, the IBSC will assess and handle applications for approval by the appropriate authorities. On a case-by-case basis, IBSC should ensure that appropriate authorities like RCGM or GEAC have given their consent before beginning rDNA work[14].

Figures 2 & 3 detail the procedures for submitting applications/reports to appropriate authorities for authorisation in the biopharmaceutical industries[14].

Fig. 2: rDNA Guidelines 2017.[12]

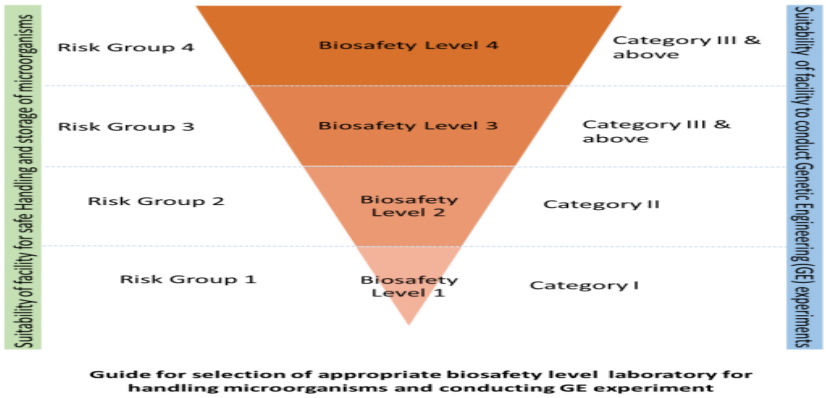

Fig. 3: Guide Selection for Biosafety Level.[14]

Regulatory Approvals Pathway

In general, the following authorities have granted permission for various sorts of research:

IBSCs Approval Process

IBSC will assess the institution's capacity to conduct the intended recombinant DNA investigations, particularly those involving high-risk species (RG3 and RG4) and activities classified as Category III and above[14].

The "Regulations and Guidelines on Biosafety of Recombinant DNA Research & Biocontainment, 2017" classified GE research into four categories (Category I, II, III, and IV), each with its own set of hazards and regulatory authorities. The types of GE research and biosafety level institutions are listed in Table 3 correspondingly, based on the microorganism engaged in the GE research to be done.

- The original study aim and study designs, as well as the microorganisms involved, must be reported to the IBSC in Category I GE research.
- Prior authorisation from IBSC is required for Category II GE studies before they may begin, and this must be obtained by submitting data in the stipulated proforma.
- Under the "Revised Simplified Procedure/Guidelines on Import, Export, and Exchange of Regulated Products, 2020," the IBSC may approve the Import/ Export/ Transfer/ Receive of regulated items in prescribed amounts for Biopharma R&D purposes of Drug Development and R&D.
- After receiving clearance from IBSC/ RCGM, the applicant must apply to the Directorate General of Foreign Trade (DGFT) of the Ministry of Commerce for the export of biological materials that fall under the Special Chemicals, Organisms, Materials, Equipment, and Technologies (SCOMET) category[14].

Table 3: Forms and Performa.[13]

I. IBSC	
Medical Surveillance Report Performa	
Confidentiality Agreement Performa, Curriculum Vitae, and Other Formats	
IBSC Minutes Format	
Annual Compliance Report Performa	
II. Import, Export, Transfer and Receive of Regulated Material Form for HMOs, GMOs/LMOs & Products thereof Application Forms for R & D Purpose	
FORM B1	For import
FORM B3	For export
FORM B5	For receiving
FORM B7	For transfer
III. Activities concerning Research, Production, Preclinical Research on GMOs in Healthcare	
FORM C1	Information to the RCGM for it to conduct research and development for medical and industrial purposes.
FORM C3a	Application to the RCGM for pre-clinical testing of similar biologics developed with GMOs for medical and commercial use
FORM C3b	For pre-clinical testing of a new DNA product
FORM C5a	For pre-clinical or other safety studies of similar biologics
FORM C5b	For pre-clinical or other safety study reports for a new rDNA product
FORM F3	For report on GE and arthropod controlled release research projects for agricultural, medicinal, and environmental purposes

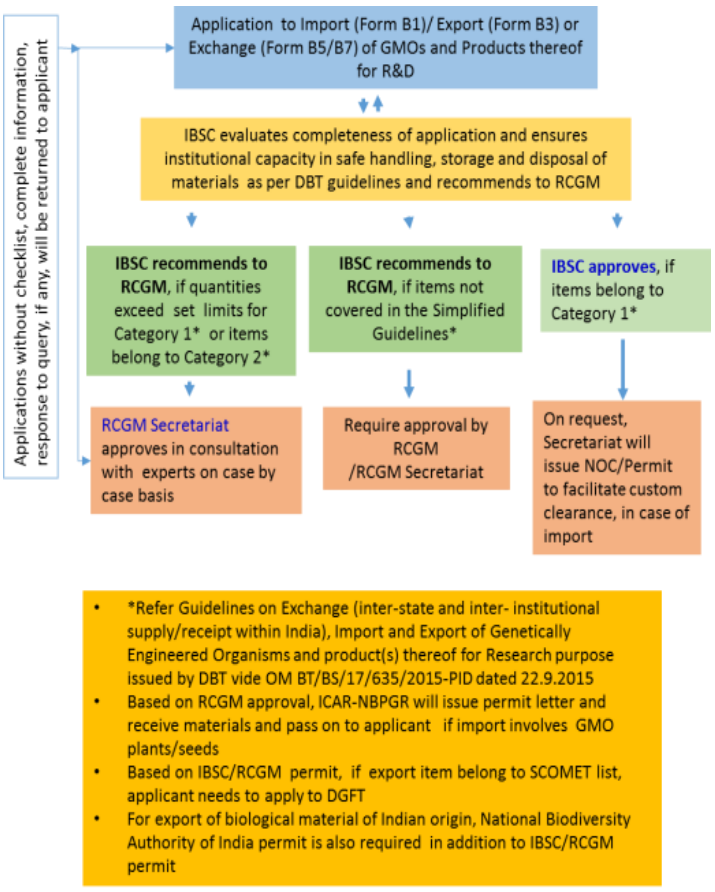

Fig. 4: Import/ Export/ Transfer/Receive of HMOS/GMOS/LMOS or cells.[14]

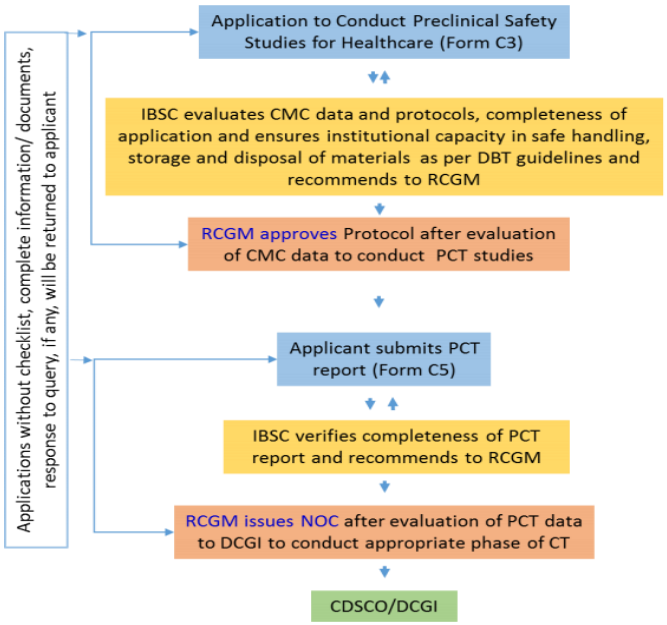

Fig. 5: Pre-Clinical & Safety Studies of Medical Products.[14]

Processing the Applications for Approval of RCGM

IBSC will examine and approve PI (sub-users) to file submissions to the RCGM for import, export, transfer, and receiving of regulated products.

1. The items which are not covered in the "Revised Simplified Procedure/Guidelines on Import, Export, and Exchange of Regulated items for R & D purpose, 2020" require approval from RCGM.
2. For Import, Export, Transfer, Receive, and Research and development activities, all materials belonging to Risk Group 3 and Risk Group 4 demand former approval from IBSC, accompanied by RCGM.
3. The investigation, manufacturing, pre-clinical studies of HMOs or GMOs in healthcare and other research are all included in Category III operations.
4. To notify the RCGM of the need to conduct R & D using HMOs, GMOs, and LMOs in the medical and related industries.
5. To apply to the RCGM for permission to perform pre-clinical and/or safety testing on similar biologics generated using HMOs or GMOs or LMOs for medical and industrial applications.
6. To apply to the RCGM for permission to perform pre-clinical and/or safety testing on new DNA items created with HMOs, GMOs, and LMOs.
7. To submit a pre-clinical or other safety research report to the RCGM for a similar biologic/new rDNA product manufactured using HMOs or GMOs, or LMOs. IBSC will appoint relevant experts to analyse PCT reports and submit them to RCGM with their comments.
8. To submit Report to RCGM on restricted release research studies of GE Arthropods for agriculture, medical and environmental use[14].

Other Approvals Required

Other regulatory authorities may need to approve GE operations in addition to IBSC and RCGM permission.

In the case of field trials, approval from the GEAC, CDSCO, Animal Ethics Committee, and NOC from the State Government is necessary[14].

Other Applicable Guidelines

IBSC can also refer following guidelines:

- "Guidelines on Similar Biologics, 2016"
- "Guidelines for Generating Pre-Clinical and Clinical Data For r-DNA Based Vaccines, Diagnostics And Other Biologicals, 1999" to provide data for pre-clinical safety evaluation in a systematic and structured

manner that covers the product's safety, purity, potency, and efficacy[14].

Offences

The following activities are considered an offence:

A. Import, export, transport, manufacture, process, use, or selling of HMOs/GMOs/LMOs without the approval of the Genetic Engineering Approval Committee
B. Experimentation on HMOs/GMOs/LMOs in non-designated facilities or unregistered institutions or labs.
C. Discharge of microorganisms/genetically engineered organisms or cells mentioned in the schedule from laboratories, hospitals, and other areas.
D. Scale-up or pilot operations without a license from the Genetic Engineering Approval Committee.

Certain studies in the field of gene technology or microorganisms for educational purposes may be conducted outside of the labs, and the laboratory will be overseen by the Institutional Biosafety Committee[9].

Penalties

In the event of a violation, the District Level Committee or the State Biotechnology Coordination Committee may pursue legal action at the offender's expense. If immediate action is required to safeguard the environment, nature, or human health, the DLC/SBCC may do so without issuing any orders or notifying the public. The individual who caused the injury will refund the fees incurred for this purpose. The SBCC/DLC may collect samples for a more in-depth examination of organisms and cells. The SBCC/DLC will be able to seek assistance from any other government entity in order to carry out its directives[9].

Bioterrorism

The Covid-19 pandemic has caused a great threat on the health and prosperity of the world. Unfortunately, microorganisms possessed by the many countries are far more dangerous than the coronavirus because of their fatality rate. The possession of these bioweapons needs to be checked. For instance, Australian scientists accidently generated a fatal mousepox virus in 2001 while trying to genetically modify the mousepox virus to make lab mice sterile. A synthetic strain of the poliovirus was created in 2002 by State University of New York researchers using chemicals and publicly accessible genetic data. And in 2005, a team of American scientists revived the virus that sparked the 1918 influenza pandemic, a disease that is thought to have killed 50 million people worldwide between 1918 and 1919. In another instance, a team at the University of Alberta purchased DNA pieces online for roughly $100,000 and used them to construct a contagious horse pox virus, a close cousin of the smallpox virus[15]. The UN is playing a vital role in keeping a check on bioterrorism by forming common guidelines for all the member countries. Bioterrorism is described as the systematic and deliberate deployment of hazardous microorganisms such as bacteria, viruses, or their toxins to spread infectious diseases on a massive scale in order to wipe out a huge population. The global incidents of the recent twenty years presented that the danger of biological fighting isn't a fictional thing yet a harsh truth. By seeing flare-ups brought about by microorganisms and terror that highly dangerous microbes can be utilised in bioterrorism. So, there is a need to improve the countermeasures to tackle the spread of infectious diseases[5].

The Biological Weapons Convention (BWC) adequately forbids the turn of events, creation, obtaining, transfer, accumulating, and utilising bioweapons. It was the primary multilateral demobilisation settlement prohibiting a whole classification of weapons of mass annihilation (WMA). The BWC is a vital component in the worldwide local area's endeavours to address WMA multiplication, and it has set up a solid standard against bioweapons. The convention has arrived at practically all-inclusive participation with 183 States Parties and four Signatory States[16].

Table 4: Key Provisions of the Convention.[16]

Article	Provision
Article I	Undertaking never under any conditions to create, produce, reserve, procure or hold bioweapons.
Article II	Undertaking to obliterate bioweapons or redirect them to peaceful purposes.
Article III	Undertaking not to move, or in any capacity helps, urge or incite anybody to fabricate or, in any case, get bioweapons.
Article IV	Prerequisite to go to any public lengths important to preclude and forestall the turn of events, creation, amassing, obtaining or maintenance of bioweapons inside a state's region, under its purview, or influenced quite a bit by.
Article V	Taking on the responsibility to advise on a bilateral and multilateral basis and participate in addressing any concerns that may arise in relation to the BWC's purpose or implementation.
Article VI	The right to ask the UN Security Council to examine verified BWC violations and to take part in any inquiry launched by the Security Council.
Article VII	Undertaking to help any State Party presented to risk because of an infringement of the BWC.
Article X	Undertaking for work with, and reserve the option to partake in, the fullest conceivable trade of hardware, materials and data for peaceful purposes.

Bioterrorism: India

India is a signatory to the BWC (Biological Weapons Convention) of 1972. In India, a very much evolved biotechnology foundation that incorporates various pharmaceutical creation laboratories and bio-regulation research facilities (counting Biosafety Level 3, i.e., BSL-3) for working with deadly microbes is in place. It likewise has qualified researchers with skill in irresistible infections. A portion of India's laboratories is being utilised to help innovative work for BW guard purposes. These offices comprise a likely significant capacity for hostile purposes too. To study biochemical pharmacology, toxicology and advancements of antibodies against a few viral and bacterial infections, DRDE - Defence Research and Development Establishment at Gwalior is the essential foundation. Innovations are going to get ready against dangers like Brucellosis, cholera, Anthrax and plague, and viral dangers like smallpox, viral fever and botulism. Analysts have created substance/organic defensive stuff, including veils, suits, locators and reasonable medications[17].

A large population, poor level of cleanliness and fewer disinfection facilities alongside amiable climatic conditions make India defenceless from the spread of irresistible sicknesses brought about by biowarfare specialists. What's more, India doesn't have satisfactory medical facilities; for example, on a normal level government can serve almost 12,000 individuals. Consequently, the vast majority of individuals stay untreated. So, the delivery and spread of illness turn out to be very simple, prompting the flare-up of bioterrorism[6].

The danger of bioterrorism has been under consideration by Indian security agencies and defence physicians for quite a while. There have been a couple of episodes that have brought doubt up previously. In the course of the Indian and Pakistan battle in 1965, a typhus attack in the north-eastern part of India caught the attention of authorities. The Indian security agencies and defence agencies were aware of the episode of the pneumonic plague (notable in biowarfare) in the Surat city of the Indian state of Gujarat and the Bubonic plague outbreak in the Beed city of the state of Maharashtra in 1994, which caused a few fatalities and ample amount of monetary loss. In 2001, the Bacillus anthracis alarm arrived at Secretariat (Mantralaya), and, even as India attempts to forestall militant psychological assaults, for example, the one in Mumbai in November 2008, security specialists say that regardless of not confronting a bioweapon assault up until this point, the nation should not overlook that threat[5].

Historical Cases of Pandemic/Epidemic by Microbes in India

The ascent and spread of irresistible sicknesses due to hazardous microorganisms have happened consistently throughout a long range of history. "Critical epidemics as well as pandemics, for instance, influenza, plague, cholera, Middle East respiratory syndrome coronavirus (MERS-CoV) and severe acute respiratory syndrome coronavirus (SARS-CoV) have effectively tormented humankind." The globe is now dealing with the new coronavirus pandemic[18].

Pandemics have happened in the past because of various illnesses, cholera, plague and Flu, specifically attacked the Indian subcontinent in the nineteenth and early twentieth century. A plague is a disease caused by bacteria; it drove the pandemic from 1896 to 1939 and was responsible for 12 million mortalities; a virus-driven infection, the Spanish Flu, caused twelve million fatalities in India in just three months in 1918[19].

The British government responded quickest on account of the plague. Given the dread that it would spread to Europe and be a repetition of the Black Death of the fourteenth century so, to tackle this, the government presented the Epidemic Diseases Act in 1897 that included large-scale clean practices - halting fairs, celebrations and journeys, truly investigating both male and female railroad travellers, sending presumed cases to the clinic, looking through homes (particularly by troops) searching for plague patients, destroying the property, forestalling entombments or incinerations except if the cause for death had been confirmed by a clinical official, etc[20].

Cholera Pandemic

Cholera is an intense, deadly sickness of the gastrointestinal tract caused by the bacteria Vibrio cholerae. It is a fatal diarrhoeal infection that can kill in no time whenever left untreated and is brought about by the consumption of food or water polluted by the bacteria Vibrio cholerae. Because of cholera, there are generally 1.3 to four million cases and 21000 to 143000 fatalities worldwide[21]. Cholera was endemic (having a place or local to a specific group or country)[22]. in Asia until 1817, when the first pandemic spread from India to different regions of the world. In the nineteenth century, cholera was transmitted all over the world from the delta of the Ganges in India. After that, six resulting outbreaks killed a large population of people. The last, i.e., the seventh pandemic, emerged from South Asia in 1961, attacked Africa in 1971 and America in 1991. Even in this current scenario, Cholera is endemic in developing countries[18].

Smallpox Pandemic

Smallpox is a contagious disease caused by virus strains Variola Major or Variola Minor, which causes a lot of pain, especially by the pustules that form on the body. Since the eighteenth century, it has been one of the most common illnesses to benefit from targeted vaccination campaigns, which have played a key role in acquiring disease immunity. In the late twentieth century, it was virtually destroyed[23].

Plague Pandemic

Plague has a lengthy history in India, dating back hundreds of years, and is most often associated with the unusual death of rodents prior to human mortality, as well as the bubo or protuberance was seen on diseased carcasses[19]. The first reported case of the bubonic plague was accounted for by the doctor A.G. Viegas in Bombay. From its beginning in China, the plague brought about by rodents biting which are contaminated by insect nibble or people coming into touch with the carcass of a tainted rat travelled across the country to Hong Kong, from there it spread to British India and other areas of the globe by ship exchange. The dissemination of plague remained a mystery until 1905, when it was discovered that the plague bacterium Yersinia pestis (found in 1894) was disseminated in humans from rodents via the bites of rodent bugs or rat's fleas. Other spreading aspects involve airborne transmission by sneezing for the case of pneumonic plague[24].

Plague yet endemic in native rat populaces of Africa and Central Asia, South and North America. In case of a pandemic, plague is communicated by chomp of Indian rodent bug. The essential hosts of the insects include earthy coloured sewer rats and dark rats. Pneumonic plague is likewise contagious because of transmission by air droplets after sneezing. Bubonic plague additionally has military importance and is recorded by the CDC USA as a Category A bioterrorism agent[25].

Influenza Pandemic

In late spring 1918, Bombay papers declared the appearance of a new infection, famously known as 'Spanish Influenza'/'Spanish Flu' This news didn't get much attention at first until it was revealed that the disease, which had been migrating from nation to country, finally landed in India. 'Bombay Fever' was the name given to it when it first appeared in Bombay. Because of the high warmth and wetness, Bombay then became "a magnificent nursery of the beginnings of disease" in June 1918, according to The Times of India on October 23, 1918[26]. The 1918 influenza outbreak was one of the worst in modern history. It was caused by an H1N1 virus that contained bird genetic material[27].

In February 1957, another flu **H2N2 virus** infection arose in East Asia, setting off a pandemic called an Asian Flu[28]. Asian Flu seems to have arrived in India through Madras in May 1957. The pandemic wave moved throughout the subcontinent in the following 12 weeks, which presented the extreme invasion of the new infection into the populace. Between May 19 1957, and February 8 1958, there were accounted 4451758 cases, with 1098 fatalities[29].

Epidemic Diseases Act of 1897: Past & Present

The Epidemic Diseases Act was passed in 1897 with the point of better forestalling the spread of "risky pandemic illnesses". It was capable of handling the scourge of bubonic plague that broke out in Bombay in 1896 at that point. The Epidemic Diseases Act is perhaps the briefest demonstration of any law in India, containing only four segments. The main segment clarifies the title and the degree, while the subsequent gives powers to the state and Central legislatures to go to exceptional lengths and plan guidelines that are to be seen by individuals to prevent the transfer of sickness. Section third depicts punishments for abusing the guidelines, as per section 188 IPC. The fourth arrangement provides legitimate assurance of protection to the executing officials acting under the Act. As per the arrangements of Section 2 that depicts the powers of the public authority, When the state government is fulfilled that the state or any part thereof is visited by or undermined with a flare-up of any hazardous scourge sickness; and assuming it believes that the standard arrangements of the law are lacking for the reason, then, at that point, the state might take, or require or engage any individual to go to certain lengths and by open public notification/notices recommend such transitory guidelines to be followed by people. The state government might recommend guidelines for examination of people going by rail line or in any case, and the isolation; in a medical clinic, in temporary shelter or any case, of people pointed out by the investigating officer with being contaminated with any such infection[30].

- Section 2A enables the Central government to assess any boat departing or showing up at any port and for confinement thereof or of any individual proposing to cruise in that or showing up in this way[31].
- Section 3 states that a half year's detainment or a thousand rupees fine or both in case of violation under the IPC 188[32].
- Section 4 of this Act protects persons acting under this, i.e., no suit or other judicial procedure will lie against any individual for anything done or in with the best of intentions expected to be done under this Act[31].

The Act was formed around 125 years prior and hence has a lot of limitations in this period of changing needs in general health crisis management. Definition of "perilous epidemic infection" isn't given in the Act. It is crucial for realising who decides on what a "hazardously pestilence sickness" is and what standards the definition depends on. The Epidemic Diseases Act is administrative and restricted in terms of public well-being concerns. It stresses the force of the public authority yet is quiet on the freedoms of residents. It has no arrangements that think about individuals' advantages. The Act is likewise quiet on the moral viewpoints or basic liberties rules that become possibly the most important factor during the response to an epidemic[30].

Conclusion

India has a well-regulated framework for the regulations of genetically engineered microorganisms, but there are no clear penalties for the offences regarding the violations of rules 1989. In India, there is no registered case

of violations or biohazard breaches from biocontainment facilities, and all the registered IBSC databases can be accessed by only principal investigators of registered IBSCs. For the general public, the data is not accessible.

Even though the regulations in India concerning GE organisms in the light of recommendations on the global level have been created on paper, their implementation on the ground level is still a big challenge. If we have a glance at the cases of breaches from labs, the data is disappointing.

Government must take bioterrorism seriously and be informed about it since it is a genuine danger. Therefore, appropriate awareness campaigns for our country's inhabitants should be put up right once. Large-scale health issues and suffering of the populace are brought on by biological weapons. This causes the government to crumble and become weak. Preventive measures and initiatives toward bioterrorism have to be enhanced, strengthened, and made more effective in a nation like India, where the population is rising daily and has surpassed a billion. To combat bioterrorism, it has become important to strengthen the regulations on advanced research on GE microorganisms and take measures to implement it on the ground level.

REFERENCES

1. Question and Answers on the regulation of GMOs in the EU What are GMOs and GMMs? Question and Answers on the regulation of GMOs in the EU What are GMOs and GMMs? European Commission, Published May 19, 2004, Accessed June 2, 2022. https://ec.europa.eu/commission/presscorner/detail/en/MEMO_04_102
2. D. J. Stemke, "Genetically Modified Microorganisms", In, S.R. Parekh (eds), ***The GMO Handbook Humana Press, Totowa, NJ,*** 85-130 (2004).
3. J. Wesseler, G. Kleter, M. Meulenbroek and K.P. Purnhagen, "EU regulation of genetically modified microorganisms in light of new policy developments: Possible implications for EU bioeconomy investments", ***Appl Econ Perspect Policy***, Early online view 2022.
4. Pharmaceutical Use of GMOs, Science of GMOs. Accessed May 29, 2022. https://gmo.uconn.edu/topics/pharmaceutical-use-of-gmos/#
5. V. Pinto, "Bioterrorism: Health sector alertness", ***J Nat Sci Biol Med,*** 4(1), 24-28 (2013).
6. K. Krishan, B. Kaur and A. Sharma, "India's preparedness against bioterrorism: biodefence strategies and policy measures", ***Curr Sci,*** 113(9), 1675-1682 (2017).
7. Ministry of environment, Forest and Climate Change, Government of India, Understanding Cartagena Protocol on Biosafety: A Guide. Published 2003. Accessed March 1, 2022. https://geacindia.gov.in/resource-documents/14-Understanding_Cartagena_Protocol_on_Biosafety_A_Guide.pdf
8. V. Ahuja, "Regulation of emerging gene technologies in India", ***BMC Proceedings,*** 12(8), 5-11 (2018)
9. Ministry of environment, Forest and Climate Change, Government of India, Notification: The Manufacture, Use, Import, Export and Storage of Hazardous Microorganisms Genetically Engineered Organisms or Cells Rules, 1989.
10. Central Pollution Control Board, Ministry of environment, Forest and Climate Change, Government of India. Accessed April 21, 2022. https://cpcb.nic.in/env-protection-act/
11. Hybridization, National Human Genome Research Institute. Accessed April 21, 2022. https://www.genome.gov/genetics-glossary/hybridization
12. Regulations and Guidelines on Biosafety of Recombinant DNA Research & Biocontainment, 2017. Accessed April 21, 2022. https://rcb.res.in/upload/Biosafety_Guidelines.pdf
13. IBK Portal, Government of India, Ministry of Science and Technology, Department of Biotechnology, Office Memorandum Accessed February 28, 2022. https://ibkp.dbtindia.gov.in/Content/Rules
14. Government of India, Ministry of Science and Technology, Department of

Biotechnology, Office Memorandum: Handbook for Institutional Biosafety Committees (IBSCs).
15. R. Langer and S. Sharma, "The Blessing and Curse of Biotechnology: A Primer on Biosafety and Biosecurity, Carnegie Endowment for International Peace. Accessed August 17, 2022. https://carnegieendowment.org/2020/11/20/blessing-and-curse-of-biotechnology-primer-on-biosafety-and-biosecurity-pub-83252
16. Biological Weapons Convention – UNODA. Accessed June 19, 2022. https://www.un.org/disarmament/biological-weapons/
17. Biological Warfare, India Nuclear Forces. Accessed June 19, 2022. https://nuke.fas.org/guide/india/bw/
18. J. Piret, G. Boivin, Pandemics Throughout History, ***Front Microbiol***, 11, 3594 (2021).
19. Tumbe. Pandemics and Historical Mortality in India tumbe, Google Search. Accessed June 19, 2022. https://web.iima.ac.in/assets/snippets/workingpaperpdf/17719931472020-12-03.pdf
20. Pandemics of the Past, India Today Insight News. Accessed June 19, 2022. https://www.indiatoday.in/india-today-insight/story/coronavirus-pandemics-of-the-past-1656730-2020-03-18
21. WHO update, Cholera, Accessed June 19, 2022.https://www.who.int/news-room/fact-sheets/detail/cholera
22. Endemic Definition & Meaning, Merriam-Webster, Accessed June 19, 2022. https://www.merriam-webster.com/dictionary/endemic
23. Pandemics and Historical Mortality in India, Google Search, Accessed June 19, 2022. https://www.google.com/search?q=Pandemics+and+Historical+Mortality+in+India+tumbe&oq=Pandemics+and+Historical+Mortality+in+India+tumbe&aqs=chrome..69i57j33i10i160l4.3972j0j4&sourceid=chrome&ie=UTF-8
24. When the 1897 bubonic plague ravaged India, Mint, Accessed June 19, 2022. https://www.livemint.com/mint-lounge/features/when-the-1897-bubonic-plague-ravaged-india-11587876174403.html
25. J. Frith, "The History of Plague – Part 1. The Three Great Pandemics", ***JMVH,*** 20(2), 11-16 2022.
26. M. Singh, "Bombay Fever/Spanish FLU: Public health and native press in Colonial Bombay, 1918–1919", ***South Asia Res,*** *41*(1), 35–52 (2021).
27. History of 1918 Flu Pandemic | Pandemic Influenza (Flu) | CDC. Accessed June 20, 2022. https://www.cdc.gov/flu/pandemic-resources/1918-commemoration/1918-pandemic-history.htm
28. 1957-1958 Pandemic (H2N2 virus)| Pandemic Influenza (Flu) | CDC. Accessed June 20, 2022. https://www.cdc.gov/flu/pandemic-resources/1957-1958-pandemic.html
29. I.G. Menon, "The 1957 pandemic of influenza in India", ***Bull World Health Organ,*** 20(2-3),199-224 (1959).
30. P.S. Rakesh, "The Epidemic Diseases Act of 1897: public health relevance in the current scenario", ***Indian J Med Ethics,*** 3, 156-160 (2016).
31. The Epidemic Diseases Act, 1897. Accessed June 20, 2022. https://indiankanoon.org/doc/1005961/
32. What is Section 188 IPC, under which you will be booked for violating COVID-19 lockdown? | Explained News,The Indian Express. Accessed June 20, 2022. https://indianexpress.com/article/explained/explained-section-188-of-ipc-under-which-you-can-be-fined-rs-1000-for-violating-lockdown-6328022/

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نشـرة العـلوم الصيدليـــــة
جامعة أسيوط

اللوائح المتعلقة بالكائنات الدقيقة المعدلة وراثيًا وعلاقتها بالإرهاب البيولوجي في الهند

جورفيندر سينغ[١*] – فيكاس بودهور[١] – مانجوشا شودري[٢] – سيكندر سينغ[٣]

[١] **قسم العلوم الصيدلانية ، جامعة ماهارشي دايانااند ، روهتاك ، ١٢٤٠٠١ ، هاريانا ، الهند**
[٢] **معهد العلوم الصيدلانية ، جامعة كوروكشيترا ، كوروكشيترا ، الهند**
[٣] **ايميل المحدودة للادوية ، نيودلهى ، الهند**

أظهرت جائحة كوفيد-١٩ للعالم المخاطر المحتملة التي تشكلها الكائنات الحية الدقيقة مثل البكتيريا والفيروسات والريكتسيا والفطريات وسمومها. ومع ذلك ، فإن الكائنات الحية الدقيقة المعدلة وراثيًا مفيدة في مختلف مجالات العلوم الحيوية ، بما في ذلك الأدوية ، والبستنة ، وأساسيات التحقيق في عمليات الحياة. بعض هذه الكائنات الحية الدقيقة المعدلة وراثيًا لها إمكانية هائلة للتسبب في ضرر للبشر ، وقد هزت البيئة ، مثل جائحة فيروس كورونا مع الوفيات الناجمة عنه في جميع أنحاء العالم ودمرت الاقتصاد العالمي. من ناحية أخرى ، تساعد الكائنات المعدلة وراثيًا في فهم البنية التحتية لهذه الكائنات كأداة لمكافحة المرض الذي تسببه. من ناحية أخرى ، تشكل الأبحاث المتزايدة حول هذا الأمر أيضًا تهديدًا لحدوث الأوبئة في جميع أنحاء العالم. في الهند ، يتم تنظيم الكائنات الحية الدقيقة المعدلة وراثيًا بموجب القواعد لعام ١٩٨٩ بموجب المادتين ٦ و ٨ و ٢٥ من قانون البيئة لعام ١٩٨٦. والإرهاب البيولوجي هو النشر المنتظم والمتعمد للكائنات الخطرة مثل البكتيريا أو الفيروسات أو السموم لنشر الأمراض المعدية في على نطاق هائل للقضاء على عدد كبير من السكان. أظهرت الأحداث العالمية في العشرين عامًا الأخيرة أن خطر القتال البيولوجي ليس شيئًا خياليًا ولكنه حقيقة قاسية. يمكن استخدام الميكروبات الخطرة في الإرهاب البيولوجي من خلال رؤية التفجيرات التي تسببها الكائنات الحية الدقيقة. لذلك ، هناك حاجة لتحسين الإجراءات المضادة للتصدي لانتشار الأمراض المعدية. يغطى هذا البحث المرجعى اللوائح المختلفة للكائنات الحية الدقيقة المعدلة وراثيًا في الهند فيما يتعلق ببيعها وتخزينها واستيرادها وتصديرها ، مع التركيز على الهيئات التنظيمية ؛ دستورها ، ونماذج طلب التسجيل والموافقة على البحث في مثل هذه الكائنات الدقيقة ، ويقدم هذا التقييم نظرة عامة واضحة على التهديدات البيولوجية المحتملة في البلاد ، والقوانين واللوائح الحالية لمكافحة مثل هذه الحوادث ، مع ضرورة كبيرة لتنفيذها ، والدفاع البيولوجي تدابير الاستعداد والدفاع ، لصالح جعل الهند دولة خالية من الإرهاب البيولوجي.